Estimated 10-year cardiovascular risk in a British population: Results of a national screening project

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Objective: To estimate 10-year cardiovascular disease (CVD) risk using the risk equation and risk categories of the Joint British Societies' Guidelines on Prevention of Cardiovascular Disease in Clinical Practice (2005).

Design: Cross-sectional CVD screening survey.

Participants: 27776 men and 43261 women aged at least 18 years.

Setting: Mobile screening clinics in 35 cities and urban conurbations in Great Britain.

Main outcome measure: Estimated 10-year risk of CVD directly standardised to the population of Great Britain.

Results: The age standardised combined prevalence of known CVD, diabetes, lipid-lowering or antihypertensive drug therapy, which invalidate multiple risk factor assessment, was 18.0% for men and 18.1% for women, after excluding 2.5% (1854/72891) of individuals with incomplete results. CVD risk was calculated for 56863 individuals, and the age-standardised prevalence of an estimated 10-year CVD risk <10% was 42.7% (95% CI 42.2, 43.1) for men and 60.4% (95% CI 60.1, 60.7) for women; 10 to <20% was 19.6% (19.1, 20.0) and 15.6% (15.2, 15.9); and ≥20% was 19.6% (19.1, 20.0) and 6.0% (5.8, 6.2), respectively. After aggregating known CVD, diabetes, antihypertensive or lipid-lowering drug therapy, or an estimated CVD risk of ≥20%, the combined standardised prevalence for individuals aged ≥50 years was 74.1% (73.5, 74.8) for men and 45.5% (44.8, 46.2) for women.

Conclusions: Using current risk thresholds, there is a substantial unmet need for primary prevention of CVD, particularly among middle-aged and elderly men.

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Development of an affordable, sensitive and rapid screening method for mutation detection in UK FH subjects

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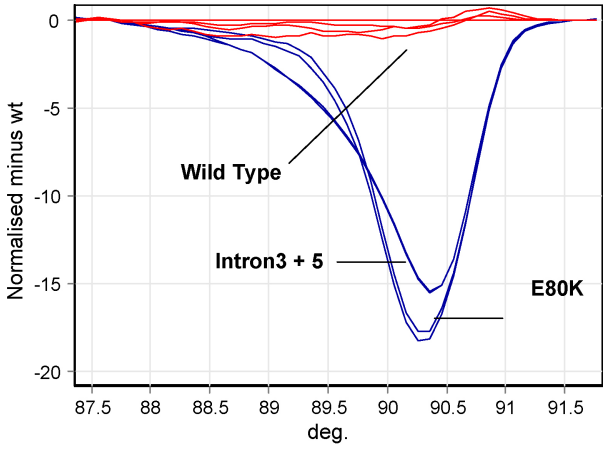
Background: Current screening methods, such as SSCP and DHPLC that are used for detecting mutations in FH subjects are time consuming, costly and only 80–90% sensitive. Here we have tested the relatively new technique of high resolution melt (HRM) analysis for mutation detection using the Rotor-Gene^{6000} real-time rotary analyser.

Methods: PCR and melt conditions for 23 fragments of the LDLR gene (4 fragments for exon 4, 2 fragments for exon 10) have been optimised. Two dyes, LCGreen and SYTO9 have been compared for sensitivity. Samples with known mutations were used as positive controls in each run. For exons with common polymorphisms which might mask an underlying mutation melt profile, genotyping was performed by RFLP so that samples could be grouped by genotype.

Results: Full analysis has been completed for exon 3 and 13. HRM was able to identify all available control mutations (exon 3 $n=10$, exon 13 $n=3$), with repeatable results on subsequent runs. In analysis of 278 FH patient samples a mutation (C47X) not previously detected by SSCP was identified. Genotyping in exon 13 for the AvaII RFLP allowed the clear detection of different mutation melt profiles in subjects of each expected genotype. Overall, the SYTO9 dye was as sensitive and is five fold cheaper than LCGreen.



Conclusions: HRM appears to be a sensitive, robust technique that could significantly reduce the time and cost of screening for mutations in a clinical setting.

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Molecular and functional analysis of a novel mutation (−139C > G) in repeat 3 of the low density lipoprotein receptor (*LDLR*) promoter gene

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Familial hypercholesterolaemia (FH) is an autosomal dominant disorder with an estimated UK prevalence of 1:500, and is associated with an increased risk for premature vascular disease. The effectiveness of DNA mutation testing versus cascade cholesterol testing is still under debate. "A comparison of DNA testing for FH with traditional diagnostic methods; Implications for cascade testing" is a current Department of Health funded study.